# FORMULATION AND EVALUATION OF LOXOPROFEN SODIUM TABLETS

Dissertation Submitted to

**The Tamil Nadu Dr. M.G.R. Medical University, Chennai – 32**

In partial fulfillment for the award of Degree of

**MASTER OF PHARMACY**

**In**

**PHARMACEUTICS**

Submitted by

**Reg. No - 26103007**

Under the guidance of

**Dr. R. Sambath Kumar. Ph.D. M.Pharm.,**

**MAY -2012**

**DEPARTMENT OF PHARMACEUTICS**

**J.K.K. NATTRAJA COLLEGE OF PHARMACY**

**Komarapalayam – 638 183**

**Tamil Nadu**

# CERTIFICATE

This is to certify that the dissertation entitled **"Formulation and Evaluation of loxoprofen sodium tablets"** is a bonafide research work carried out by **MAHESH KUMAR.K**, [Reg.No: 26103007] in the Department of Pharmaceutics under my guidance and Supervision for the partial fulfillment for the award of the Degree of Master of Pharmacy in J.K.K.Nattraja College of Pharmacy during the academic year 2011 - 2012.

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# DECLARATION

The work presented in this dissertation entitled "**Formulation and Evaluation of loxoprofen sodium tablets"**was carried out by me under the direct supervision of **Dr.R. Sambath Kumar, Ph.D. M.Pharm.,** HOD & Profesor, Department of Pharmaceutics, J.K.K.Nattraja College of Pharmacy, Komarapalayam, in the partial fulfillment for the award of the degree of Master of Pharmacy in Pharmaceutics.

This work is original and has not been submitted in part or full for the award of any other degree or diploma of any university.

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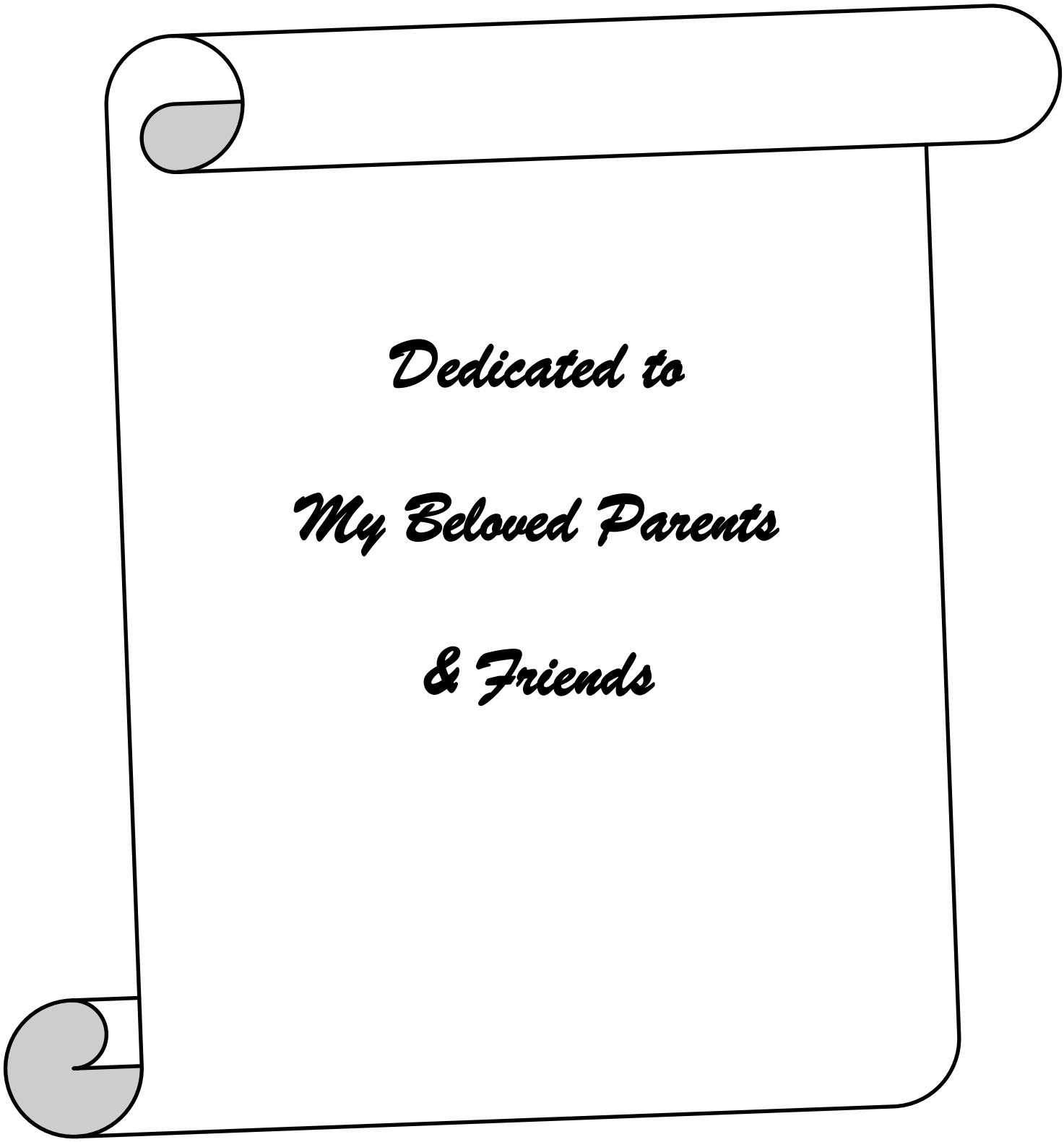
Dedicated to
My Beloved Parents
& Friends

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The best new therapeutic entity in the world is of little value without an appropriate delivery system. Tablet delivery systems can range from simple immediate release formulations to complex extended or modified release dosage forms. The most important role of drug delivery system is to get the drug delivered to the site of action in sufficient amount and at the appropriate rate; however it must also meet a number of other essential criteria. These include physical and chemical stability, ability to be economically mass produced in a manner that assures the proper amount of drug in each and every dosage form and in each batch produced and as far as possible patient acceptability the drug and the delivery systems cannot be separated.[1-2]

The general design criteria for tablet are given below[4]

1.) Optimal drug dissolution and hence availability of drug from dosage form for absorption consistent with internal use (i.e. immediate or extended release)
2.) Accuracy and uniformity of drug content
3.) Stability, including the stability of the substance, the overall tablet formulation, disintegration and the rate and extent of drug dissolution from the tablet for an extended period.
4.) Patient acceptability: as much as possible, the finished product should have an attractive appearance, including color, size, taste etc. as applicable, in order to maximize patent acceptability and encourage compliance with prescribed dosing regimen .
5.) Manufacturability: The formulation design should allow for the efficient, cost effective practical production of the required batches.

## SOLID DOSAGE FORMS[2,3]

Solid dosage forms are widely prevalent due to their age-old application. Especially, oral solid formulations hold a high potential as they serve to be most convenient for the administration of drugs. These have been developed into a wide range of formulations from conventional dosage forms for immediate release of the drug to controlled release dosage forms for the constant rate of drug release. Oral route is the most convenient and commonly used method of drug delivery. More than 50% of drug delivery systems available in the market are oral drug delivery systems. They

offer convenience and ease of administration, greater flexibility in dosage form design and ease of production and low cost. Pharmaceutical oral solid dosage forms have been used widely for decades mainly due to their convenience of administration and their suitability for delivery of drugs for systemic effects. The most commonly used pharmaceutical solid dosage forms today include granules, pellets, tablets and capsules.

**TABLET**

**Definition:[1]**

Tablets are tamperproof solid unit dosage forms containing medicament or mixture of medicaments and excipients compressed or moulded into solid cylindrical shape having either flat or convex surfaces.

## Advantages of the Tablets[1]

- They are unit dosage form, and they offer greatest capabilities of all oral dosage forms for the greatest dosage precision and the least content variability.
- Their cost is lowest of all the dosage forms.
- They are the lightest and most compact of all the dosage forms.
- They are in general the easiest and cheapest to package and ship of all oral dosage forms.
- They may provide the greatest ease of swallowing with the least tendency for "hang-up" above the stomach, especially when coated, provided that tablet disintegration is not excessively rapid.
- They lend themselves to certain special release profile products, such as enteric or delayed release products.
- They are better suited to large-scale production than the other unit oral forms.
- They have the best-combined properties of chemical, mechanical and microbiological stability of all the oral forms.

## Disadvantages of the Tablets[1]

- Some drugs resist compression into dense particles, owing to their amorphous nature or flocculent, low-density character.

- Drugs with poor wetting, slow dissolution properties, intermediate to large dosages, optimum absorption high in the GIT, or any combination of these features may be difficult or impossible to formulate and manufacture as a tablet.
- Bitter tasting drugs with an objectionable odor, or drugs that are sensitive to oxygen or atmospheric moisture may require encapsulation or entrapment prior to compression.

## Types and classes of Tablets[4]

(A) Oral tablet for ingestion

1. Compressed tablets
2. Multiple compressed tablets
3. Delayed action tablets
4. Sugar coated
5. Film coated tablets
6. Chewable tablets

(B) Tablet used in oral cavity

1. Buccal tablets
2. Sublingual tablets
3. Troches and Lozenges
4. Dental cones

(C) Tablet administered by other routes

1. Implantation tablets
2. Vaginal tablets

(D) Tablets used to prepare solution

1. Effervescent tablets
2. Dispensing tablets
3. Hypodermic tablets
4. Tablet triturates

## OPERATIONS INVOLVED IN TABLET MANUFACTURING:[5]

The manufacture of oral solid dosage forms such as tablets is a complex multi-stage process under which the starting materials change their physical characteristics a number of times before the final dosage form is produced.

The following operations are involved in tablet manufacturing:

- Dispensing
- Sifting
- Dry mixing
- Granulation
- Drying
- Milling
- Blending
- Compression
- Coating
- Packing

### . DISPENSING:

- Dispensing is the first step in any pharmaceutical manufacturing process. Dispensing is one of the most critical steps in pharmaceutical manufacturing; as during this step, the weight of each ingredient in the mixture is determined according to dose.
- Dispensing can be done by purely manual by hand scooping from primary containers and weighing each ingredient by hand on a weigh scale on mechanical devices according to BPR specification.
- Issues like weighing accuracy, dusting control (laminar air flow booths, glove boxes), during manual handling lot control of each ingredient, material movement into and out of dispensary should be considered during dispensing.
- There should be no due for calibration of the balance and zero error must be ensured in the balance.
- Ensure the expiry date of XXX is later than that of the batch expiry date and retest date is older than day of dispensing.
- Ensure all the materials are issued as per BPR.

## SIFTING:

Size plays an important role in the homogeneity of the final product. When large differences exist between the active ingredient and excipients mutual sieving (demixing) effects can occur making thorough mixing difficult during the subsequent processing steps.

Size can also be a factor in the stability. Fine materials are relatively more open to attack form atmospheric oxygen, heat, light, humidity and interacting excipients than coarse materials. Because of these significant roles it is important to decide on a desired size range, and hence to maintain and control it.

Factors to be considered during sifting:

- Check and record the temperature and relative humidity in process area. Temperature should be 25±2$^{oc}$ and RH 45±5%.
- Check and ensure visually all the equipments and equipment parts are cleaned, record remarks if any.
- Check and record the integrity of the sieves before and after sifting through out the processing activity.

## MIXING:

Mixing is defined as the process that tends to result in the randomization of dissimilar particles within a system. Dry mixing is generally carried out in a Rapid Mixer Granulator. Dry mixing involves the mixing of ingredients before adding the granulation or binder solution.

## GRANULATION:[2]

Granulation is a process of size enlargement whereby small particles are gathered into larger aggregates in which the original particles can still be identified. Granulation usually refers to processes where agglomerates with sizes ranging from 0.1 to 2.0 mm are produced.

The objectives for granulation are:

- improve the flow properties of the mix
- uniformity of the dose
- prevent segregation of the ingredients

- reduce dust during handling

Materials intended for compaction into tablet must possess two characteristics-

***Fluidity***-Good flow properties are essential for the transport of the material through the hopper into and through the feed frame & into the dies. The ideal physical form for this purpose is spheres , since these offer minimum contact surfaces between themselves & with the walls of the machine parts.

***Compressibility***-It is the property of forming stable, compact mass when pressure is applied.

Hence granulation is a vital step in tablet manufacturing.

Granulation techniques can be broadly classified into three types.

- Wet granulation
- Dry granulation
- Direct compaction

## Wet granulation

When powders are very fine, fluffy, will not stay blended, or will not compress, then they must be granulated, it means that the required quantity of powder physically will not fit into the die cavity on the tablet press. The volume of fill (bulk density) is greater than that which is mechanically allowed.

Wet granulation, the process of adding a liquid solution to powders, is one of the most common ways to granulate where the liquid solution/suspension can be either aqueous based or non aqueous based. . Water mixed into the powders can form bonds between powder particles that are strong enough to lock them together. However, once the water dries, the powders may fall apart. Therefore, water may not be strong enough to create and hold a bond. In such instances, a liquid solution that includes a binder (pharmaceutical glue) is required. Once the solvent has been dried and the powders have formed a more densely held mass, then the mass is milled. This process results in the formation of granules.

**Types of Binders**

Some binders, called wet binders, only work when added as a solution. Dry binders are preprocessed powders that when mixed with other powders help bind the ingredients together. Binders that can be used wet or dry are also available.

Eg: starch, starch derivatives, cellulose derivatives, alginate derivatives, sorbitol, povidone (PVP) etc.

Wet granulation offers a wide range of capabilities for forming granules, from the production of light granules to the production of very dense granules. More than 70% of the global industry's granulations are made using this method.

## Important steps involved in the wet granulation:

- Mixing of the drug(s) and excipients.
- Preparation of binder solution.
- Mixing of binder solution with powder mixture to form wet mass.
- coarse screening of wet mass using a suitable sieve.(#6-#12)
- Drying of moist granules.
- screening of dry granules through a suitable sieve(#14-#20)
- Mixing of screened granules with disintegrants, glidant and lubricant.

## Preparing the damp mass:

A liquid binder is added to the powder mixture to facilitate the adhesion of the powder particles. a good binder results in appropriate tablet hardness and does not negatively impact on the release of the drug from the tablet.

## Determining the End point of granulation:

A rough way of determining the end point to press a portion of the mass in the palm of the hand, if the ball crumbles under moderate pressure ;the mixture is ready for the next stage in processing , which is wet screening.

Relation between power consumption and granule formation:

The energy consumption by wet granulation (i.e.; the cumulative power consumption.)is converted completely into heat. The particles get heated up as coalescence of agglomerates becomes significant. Because of high agglomerates deformability the energy consumption will increase accordingly.

The power used by the mixer increases as the powder mass becomes increasingly wet. Power usage is often reflected in the readings of an ammeter or wattmeter mounted on the equipment and may be useful in helping to identify the proper end point for the wet granulation process.

Care must be exercised not to over wet or under wet the powder. Over wetting can result in granules that are too hard for proper tabletting.

Under wetting can result in tablets that are too soft and may tend to crumble.

## Screening the damp mass into granules:

The wet mass is passed through a screen (usually no. # 6 or 8 mesh) to prepare the granules. This may be done by hand or by special equipment which prepares the granules by extrusion through perforations in the apparatus. The resultant granules are spread evenly on large pieces of paper in shallow trays and dried.

## Dry granulation

The dry granulation process is used to form granules without using a liquid solution because the product to be granulated may be sensitive to moisture and heat. Forming granules without moisture requires compacting and densifying the powders.

Dry granulation can be conducted on a tablet press using slugging tooling or on a roller compactor commonly referred to as a chilsonator. When a tablet press is used for dry granulation, the powders may not possess enough natural flow to feed the product uniformly into the die cavity, resulting in varying degrees of densification. The roller compactor uses an auger feed system that will consistently deliver powder uniformly between two pressure rollers.

The powders are compacted into a ribbon or small pellets between these rollers and milled through a low-shear mill. When the product is compacted properly, then it can be passed through a mill and final blend before tablet compression.

Material feed rates are critical for attaining the final objective. The process may require repeated compaction steps to attain the proper granular end point. If fines are not removed or reprocessed, then the batch may contain too many of them, a situation that can contribute to capping, laminating, weight, and hardness problems on the tablet press. Roller compacting the complete formula is not usually necessary. The object is to densify powders and form granules of the products in the formula that must be compacted, mill the granules, and then blend them back in with the rest of the formula's ingredients. Most dry-granulated products do not have problems with picking and sticking because moisture is not present.

When products are dry granulated, the process times are often reduced and equipment requirements are streamlined; therefore, the cost is reduced. However, dry granulation often produces a higher percentage of fines or no compacted products, which can lead to compromised tablet quality or yield problems if the product is not compacted correctly.

## Direct compaction

The drug & all the excipients are blended together and then compressed. This technique is applicable to those substances which can be directly compressed (eg. sodium chloride, sodium bromide & potassium bromide).

**DRYING:**[5]

Drying is defined as the removal of a liquid from a material by the application of heat and is accomplished by the transfer of a liquid from a surface into an unsaturated vapor phase.

## Steps followed in drying:

- Check and ensure the integrity of the FBD bag.
- Initially dry the wet granules with air for 10 minutes, till the odor of IPA is eliminated.
- Dry the granules as per BPR instructions.
- Check the LOD of granules.
- Check and ensure the dried granules are not stored above 25ºC before the milling is started.
- Check the integrity of the sieves before and after sieving.
- Collect the weight of sifted and dried granules.

## Sizing the Granulation by dry screening:

After drying, the granules are passed through a screen of a smaller mesh than used to prepare the original granulations. The degree to which the granules are reduced depends upon the size of the punches to be used. In general, the smaller the tablet to be produced, the smaller are the granules used. Screens from 12 to 20 mesh size are generally used for this purpose. Sizing of the granules is necessary so that the die cavities for the free flowing granulation. Voids or air spaces left in too large granulation would result in the production of uneven tablets.

## Blending and Lubrication:

After dry screening, a dry lubricant is coated over the granules by blending the lubricant with the granules. The powder/granules blending are involved at stage of pregranulation and/or post granulation stage of tablet manufacturing. Each process of mixing has optimum mixing time and so prolonged mixing may result in an undesired product. So, the optimum mixing time and mixing speed are to be evaluated.

Blending step prior to compression is normally achieved in a simple tumble blender. The blender may be mixed blender into which the powder are charged, blended and discharged. In special cases of mixing a lubricant, over mixing should be particularly monitored.

The various blenders used include Double cone blender, 'V' blender, Octagonal blender, Container blender, Tumbling blender, Agitated powder blender, etc.

Lubricants contribute to the preparation of compressed tablets in several ways.

- They improve flow of the granulation in the hopper to the die cavity.
- They prevent the adhesion of the tablet formulation to the punches and dies during compression.
- They reduce friction between the tablet and the die wall during the tablet's ejection from the tablet machine.
- They give sheen to the finished tablets.

## Factors to be considered in Granulation:

**MIXING TIME:**

The mixing time also determines quality of the granules.

If wet mixing time is high the tablet may fail the dissolution test since drug release from hard granules is late.

**IMPELLER MOVEMENT**

Adhesion of wetted mass to the vessel is less if impeller movement is helical. This gives a narrower granule size and few lumps.

## Factors to be considered during drying:

**Loss on Drying:**

LOD, is an expression of moisture content on a wet- weight basis, which is calculated as

$$\% \text{ LOD} = \frac{\text{wt. of water in sample}}{\text{Total wt. of wet sample}} \times 100$$

The moisture in a solid can be expressed on a wet – weight or dry – weight basis. On wet – weight basis, the water content of a material is calculated as the

percentage of the weight of the wet solid, whereas on dry – weight basis, the water is expressed as a percentage of the weight of the dry solid.

**Moisture Content:**

Measurement of the moisture in wet a solid is calculated on a dry – weight basis.

$$\% MC = \frac{\text{wt of water in sample}}{\text{Wt. of dry sample}} \times 100$$

**Milling**

Milling is the mechanical process of reducing the particle size of solids.

Milling equipment is usually classified as

| | |
|---|---|
| COARSE | # 20 mesh |
| INTERMEDIATE | # 20 -200 mesh |
| FINE MILLING | < # 200 mesh |

**Pharmaceutical Applications:**

- The control of particle size and specific surface affects the therapeutic efficiency of medical compounds.
- The drying of wet masses may be facilitated by milling, which increases the surface area and reduces the distance, the moisture must travel within the particle to reach the outer surface.
- Milling enables the free flow of powder to produce tablets of uniform weight.
- The mixing and blending of several solid ingredients of a pharmaceutical is easier and more uniform if the ingredients are approximately of the same size.

**TABLET COMPRESSION:[2]**

After the preparation of granules (in case of wet granulation) or slugs (in case of dry granulation) or mixing of ingredients (in case of direct compression), they are compressed to the final product.

There are a number of types of tablet presses or tableting machines, each varying in productivity but similar in basic function and operation. They all compress a tablet formulation within a steel die cavity by the pressure exerted by the movement of two steel punches, lower punch and an upper punch. It 'squeezes' the ingredient into the required tablet shape with extreme precision. It can make the tablet in many

shapes, although they are usually round or oval. Also, it can press the name of the manufacturer or the product into the top of the tablet.

The operation of a single punch describes the basic mechanical process.

## Stages occurring during compression:-

- Stage1: Top punch is withdrawn from the die by the upper cam .bottom punch is low in the die so the powder falls in through the hole and fills the die.
- Stage 2: Bottom punch moves up to adjust the powder weight it raises and expels some powder.
- Stage 3: Top punch is driven into the die by upper cam. Bottom punch is raised by lower cam. Both punch heads pass between heavy rollers to compress the powder ie. compression & consolidation takes place.
- Stage 4: The upper cam withdraws top punch & lower punch is pushed up and expels the tablet ie. ejection takes place. Tablet is removed from the die surface-by-surface plate.
- Stage 5: Return to stage 1.
- Rotary tablet machines equipped with multiple punches operate through the continuous rotating movement of the punches.

## Factors to be considered during compression:

- Check and ensure the temperature and relative density humidity of the compression room is not more than 25ºC and RH not more than 50%.
- Check and ensure the compression machine is cleaned as per BPR.
- Collect 40 tablets and inspect for appearance, weight, thickness, friability and hardness every 1-hour and every break as per BPR.
- Tablet weight variation, hardness & thickness should be within the limit as per BPR.
- Collect 40 by "Bracketting" i.e., by increasing this speed of the compression machine from the target speed and by reducing the speed by 4 rpm.
- Collect 10 tablets during initial, middle and end of the compression process and conduct analysis for content uniformity and assay.

# TABLET COATING:

Tablet coating is the application of coating composition to moving bed of tablets & concurrent use of heated air to facilitate evaporation of solvent.

## FILM COATING:

Film coating is deposition of thin film of polymer surrounding the tablet core. Conventional pan equipments may be used but now-a-days more sophisticated equipments are employed to have a high degree of automation and quality coating. The polymer is solubilised in solvent & other additives like plasticizers and pigments are added. Resulting solution is sprayed onto a rotated tablet bed. The drying conditions cause removal of the solvent, giving thin deposition of coating material around each tablet.

### Factors to be considered during coating process:

- Check and ensure the coating pan and other equipments are cleaned as per BPR.
- Check and ensure that the speed of the coating pan, gun to bed distance, inlet and exhaust air temperature, spray rate, spray type, number of guns, temperature of the coating solution are as per BPR instruction.
- After coating is completed, samples are collected for dissolution testing and weight variation.

### Coating parameters to be considered:

- Spray gun model
- Pan load (kg)
- Pan speed (rpm)
- Spray procedure
- Spray rate (g/min)
- No. of spray guns
- Distance between spray guns (cm))
- Distance between spray gun & tablet bed
- Main inlet pressure ($kg/cm^2$)
- Atomization pressure ($kg/cm^2$)
- Inlet air temperature ($^oC$)

- Tablet bed temperature (ºC)
- Position of dampers - inlet
  - Outlet
  - % inlet / % outlet
- Quantity of coating suspension in the liquid vessel (kg/ltr)
- Average weight preheated core tablets (mg)

## PROCESS VARIABLES DURING FILM COATING

The variables to be controlled during pan spray film coating processes are:

1. **Pan variables:**
   - Pan design/baffling
   - Speed
   - Pan load
2. **Process- Air**
   - Air quality
   - Temperature
   - Airflow rate/volume/balance
3. **Spray variables**
   - Spray rate
   - Degree of atomization
   - Spray pattern
   - Nozzle to bed distance

# LITERATURE REVIEW

**Mahesh Kumar S et al; In Vitro and In Vivo Studies on HPMC-K-100 M Matrices Containing Loxoprofen Sodium;** Drug Delivery, Volume 14, Issue 3 March 2007 , pages 163 – 169

Controlled release (CR) matrix tablets of loxoprofen sodium were prepared by wet granulation using hydroxypropyl methyl cellulose (HPMC-K-100 CR) as the hydrophilic rate controlling polymer. The effect of the concentration of the polymer and different fillers on the in vitro drug release rate was studied. The studies indicated that the drug release can be modulated by varying the concentration of the polymer and the fillers. An optimized formulation subjected to accelerated stability studies for 3 months revealed that the developed CR tablets are stable. A complete cross-over bioavailability study of the optimized formulation of the developed CR tablets and marketed immediate release tablets was performed in 6 healthy male volunteers. The extent of absorption of drug from the CR tablets was significantly higher than that for the marketed loxoprofen sodium tablet due to lower elimination rate and longer half-life.

**Dahl T et al; Effects of various granulating systems on the bioavailability of loxoprofen sodium from polymeric matrix tablets;** Journal of Pharmaceutical Sciences, Volume 79, Issue 5,Sep 2006, Pages 389 – 392.

Loxoprofen sodium and a cellulose ether derivative were granulated with either water or a poly(meth)acrylic acid ester copolymer aqueous dispersion to make three controlled-release matrix dosage forms. The different polymeric matrix systems contained hydroxypropyl methylcellulose (formulation A), hydroxypropylcellulose: poly-(meth)acrylic acid ester copolymer (formulation B), and hydroxypropyl methylcellulose:poly(meth)acrylic acid ester copolymer (formulation C). All three hydrophilic matrix tablets demonstrated identical in vitro dissolution rates. The three controlled-release formulations were compared with a marketed immediate-release loxoprofen sodium dosage form (formulation D) in a single-dose crossover study in six healthy volunteers.

**Piera Di Martino et al; Physico-chemical and technological properties of sodium loxoprofen granules prepared in a high-shear mixer-granulator;** Journal of Pharmaceutical Sciences, Volume 97, Issue 12, Apr 2008, Pages 5263-5273.

In the present work, authors produced tablets of anhydrous sodium loxoprofen by wet granulation using a high-shear mixer-granulator. Drug hydrated to the tetrahydrated form, as observed by X-ray powder diffractometry.

**Young-soo Kim et al; Solubility and prediction of the heat of solution of sodium loxoprofen in aqueous solutions;** Journal of Pharmaceutical Sciences, Volume 94, Issue 9, July 2005, Pages 1941-1948

The solubility of sodium loxoprofen was determined over a range of temperatures from 15.2°C to 39.7°C by two methods: analyses of samples from equilibrated solutions and a recently developed procedure utilizing a focused-beam reflectance method (FBRM).

**Hui Cao et al; Preparation a novel pH-sensitive blend hydrogel based on polyaspartic acid and ethylcellulose for controlled release of loxoprofen sodium;**Journal of Applied Polymer Science, Mar 2009

Hydrogels based on pH-sensitive polymers are of great interest as potential biomaterials for the controlled delivery of drug molecules. In this study, a novel, pH-sensitive hydrogel was synthesized by poly(aspartic acid) (PASP) crosslinked with 1,6-hexanediamine and reinforced with ethylcellulose (EC).

**Piera Di Martino et al; A new tetrahydrated form of sodium loxoprofen;** Journal of Pharmaceutical Sciences, Volume 96, Issue 1, Sep 2006, Pages 156-157.

The anhydrous sodium loxoprofen (ASN) can form several hydrated phases if maintained at different relative humidities (RH). The water uptake can promote crystallographic modifications, according to the amount of water. In a previous work, the authors showed that a dihydrated form could be obtained either by crystallization in water or by exposure of the anhydrous form to a RH of 55%. In the present work, the authors report about the formation and characterization of a new tetrahydrated form, obtained by exposing the ASN to RH $\geq$ 75%. All the hydrated compounds were characterized by the combined use of several spectroscopic, thermal, and

crystallographic techniques. The thermal stability of both the dihydrated and tetrahydrated compounds was also tested.

**Terry M. Phillips et al; Measurement of loxoprofen in human plasma by chip-based immunoaffinity capillary electrophoresis;** Biomedical Chromatography**,** Volume 20, Issue 6-7**,** Jun 2006,Pages 662 – 667

An electrokinetic immunoassay performed in a chip-based capillary electrophoresis system is described for the rapid measurement of loxoprofen in human plasma. The system employs a fluorescently labeled antibody to capture and detect the analyte of interest within a 5 min total assay time with an LOD of 0.025 µg/mL and a saturation level of 450 µg/mL. The system compared well with a conventional HPLC technique but was found to be much faster. Application of the electrokinetic assay to the study of patients with allergy to loxoprofen demonstrated increased concentrations of the drug extending past the predicted elimination half-life. The portability of the system and its ability to process up to 18 samples per hour makes it suitable for use in emergency room situations.

# AIM AND OBJECTIVE

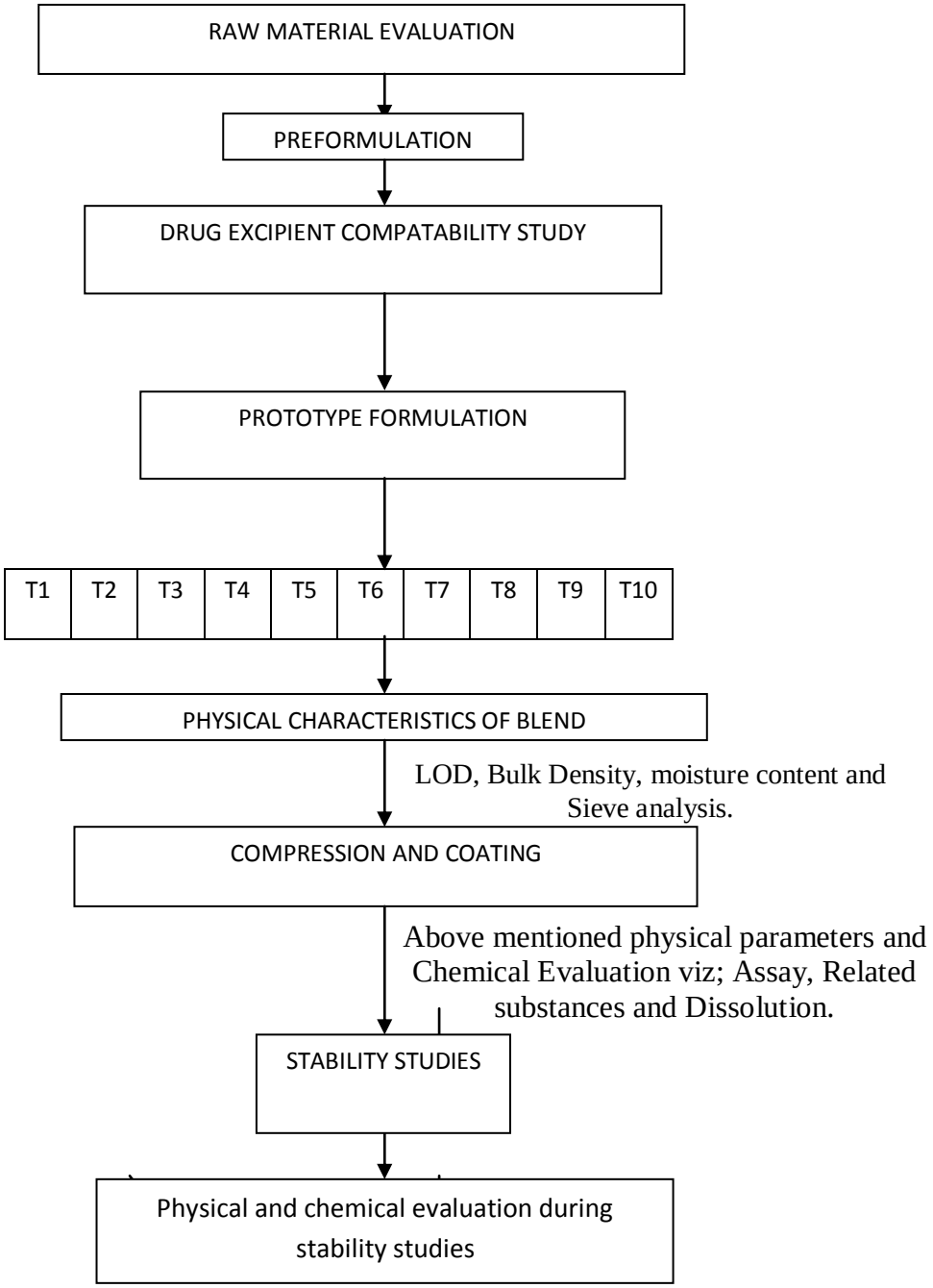
## AIM:

- The main aim of the study to formulate and evaluate loxoprofen sodium tablets.

## OBJECTIVE:

- The objective of the present study is to develop a pharmaceutically stable and robust formulation of Loxoprofen sodium tablets comparable with innovator.
- To achieve this goal various prototype trials are taken & evaluated with respect to various quality parameters.
- The formulation shall be finalized by comparing the in - vitro dissolution profile with that of the innovator in various pH media.

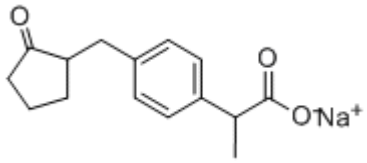
## PLAN OF WORK


RAW MATERIAL EVALUATION
PREFORMULATION
DRUG EXCIPIENT COMPATABILITY STUDY
PROTOTYPE FORMULATION
T1
T2
T3
T4
T5
T6
T7
T8
T9
T10
PHYSICAL CHARACTERISTICS OF BLEND
LOD, Bulk Density, moisture content and Sieve analysis.
COMPRESSION AND COATING
Above mentioned physical parameters and Chemical Evaluation viz; Assay, Related substances and Dissolution.
STABILITY STUDIES
Physical and chemical evaluation during stability studies

# DRUG PROFILE

**Loxoprofen Sodium**[7,8]

**Structure:**




**Chemical Formula** : $C_{15}H_{17}NaO_3$,

**Description** : Loxoprofen sodium is an odorless crystalline powder, white to creamy in color.

**Solubility** : It is soluble in methanol and water.

**Molecular Weight** : 268.28

**Category** : A member of the aryl acetic acid group of non-steroidal anti-inflammatory drugs (NSAIDs).

**Storage** : Store at controlled room temperature, 20° - 25° C (68° - 77° F). Dispense in a well-closed container.

**Actions:**

Loxoprofen is a non-steroidal anti-inflammatory drug (NSAID), with analgesic and antipyretic properties. As with other NSAIDs, its mode of action is not fully understood; however, its ability to inhibit prostaglandin synthesis may be involved in anti-inflammatory effect.

**Pharmacokinetics**:[7,8,11]

Although loxoprofen itself is well absorbed, the sodium salt form is more rapidly absorbed resulting in higher peak plasma levels for a given dose. After oral administration, plasma levels of loxoprofen are detected within 30 minutes of dosing, with peak plasma levels occurring approximately 5 hours after dosing. The observed terminal elimination half-life of loxoprofen from loxoprofen sodium tablets is approximately 15 hours. Steady state levels of loxoprofen are achieved in 3 days and the degree of loxoprofen accumulation in the blood is consistent with this.

**Absorption**

Loxoprofen itself is rapidly and completely absorbed from the GI tract with an *in vivo* bioavailability of 95%. Based on the pharmacokinetic profile, the absorption phase of tablets occurs in the first 4-6 hours after administration. . In common with conventional loxoprofen and loxoprofen sodium formulations, food causes a slight decrease in the rate of loxoprofen absorption.

**Distribution**

Loxoprofen has a volume of distribution of 0.16 L/kg. At therapeutic levels, loxoprofen is greater than 99% albumin-bound. At doses of loxoprofen greater than 500 mg/day, there is a less than proportional increase in plasma levels due to an increase in clearance caused by saturation of plasma protein binding at higher doses. However the concentration of unbound loxoprofen continues to increase proportionally to dose

**Metabolism**

Loxoprofen is extensively metabolized to 6-0-desmethyl loxoprofen and both parent and metabolites do not induce metabolizing enzymes.

**Elimination**

The elimination half-life of Loxoprofen is approximately 15 hours. Steady state conditions are attained after 2-3 doses of Loxoprofen Tablets. Most of the drug is excreted in the urine, primarily as unchanged loxoprofen (less than 1%), 6-0-desmethyl loxoprofen (less than 1%) and their glucuronide or other conjugates (66-92%). A small amount (< 5%) of the drug is excreted in the feces. The rate of excretion has been found to coincide closely with the rate of clearance from the plasma. In patients with renal failure, metabolites may accumulate.

**Indication:**

Tablets are indicated for the treatment of,

- Rheumatoid arthritis,
- Osteoarthritis,
- Ankylosing spondylitis,
- Tendinitis,

- Bursitis
- Acute gout.

It is also indicated in the relief of mild to moderate pain and the treatment of primary dysmenorrhea. Rheumatoid Arthritis, Osteoarthritis, and Ankylosing Spondylitis

**Drug Interactions:**

**ACE-inhibitors**

Reports suggest that NSAIDs may diminish the anti-hypertensive effect of ACE-inhibitors. This interaction should be given consideration in patients taking NSAIDs concomitantly with ACE-inhibitors**.**

**Aspirin**

When Loxoprofen is administered with aspirin, its protein binding is reduced, although the clearance of free Loxoprofen is not altered. The clinical significance of this interaction is not known; however, as with other NSAIDs, concomitant administration of loxoprofen and aspirin is not generally recommended because of the potential of increased adverse effects.

**Diuretics**

Clinical studies, as well as post-marketing observations, have shown that Loxoprofen can reduce the natriuretic effect of furosemide and thiazides in some patients. This response has been attributed to inhibition of renal prostaglandin synthesis. During concomitant therapy with NSAIDs, the patient should be observed closely for signs of renal failure, as well as to assure diuretic efficacy.

**Lithium**

NSAIDs have produced an elevation of plasma lithium levels and a reduction in renal lithium clearance. The mean minimum lithium concentration increased 15% and the renal clearance was decreased by approximately 20%. These effects have been attributed to inhibition of renal prostaglandin synthesis by the NSAID. Thus, when NSAIDs and lithium are administered concurrently, subjects should be observed carefully for signs of lithium toxicity.

**Methotrexate**

NSAIDs have been reported to competitively inhibit methotrexate accumulation in rabbit kidney slices. This may indicate that they could enhance the

toxicity of methotrexate. Caution should be used when NSAIDs are administered concomitantly with methotrexate.

**Warfarin**

The effects of warfarin and NSAIDs on GI bleeding are synergistic, such that users of both drugs together have a risk of serious GI bleeding higher than users of either drug alone.

**Adverse Effects:**

The most frequent adverse events are headache, followed by dyspepsia, and flu syndrome

Others include:

- Body as a Whole- Pain (back), pain, infection, fever, injury (accident), asthenia, pain chest, headache (15%), flu syndrome (10%).
- *Gastrointestinal*- Nausea, diarrhea, constipation, abdominal pain, flatulence, gastritis, vomiting, dysphagia, dyspepsia (14%), heartburn, stomatitis.
- *Hematologic*- Anemia, ecchymosis.
- *Respiratory*- Pharyngitis, rhinitis, sinusitis, bronchitis, cough increased.
- *Renal*- Urinary tract infection, cystitis.
- *Dermatologic*- Skin rash, skin eruptions, ecchymoses, purpura.
- *Metabolic and Nutrition*- Peripheral edema, hyperglycemia.
- *Central Nervous System*-Dizziness, paresthesia, insomnia, drowsiness, lightheadedness.
- *Cardiovascular*- Hypertension, edema, dyspnea, palpitations.
- *Musculoskeletal*- Cramps (leg), myalgia, arthralgia, joint disorder, tendon disorder.
- *Special Senses*- Tinnitus, hearing disturbances, visual disturbances.
- *General*- Thirst.

# CHARACTERIZATION OF INNOVATOR PRODUCT

## Description of innovator product:

**Product Name** **:** Aleve

**Expiry Date** **:** May 2010

**Distributed by** **:** Bayer Healthcare LLC, USA

**Composition** **:**

**Table-1: Composition Of Innovator Product**

| S.no | Excipients in Aleve |
|---|---|
| 1 | FD&C Blue #2 |
| 2 | Hypromellose |
| 3 | Magnesium stearate |
| 4 | Micro Crystalline Cellulose |
| 5 | Povidone |
| 6 | Poly ethylene glycol |
| 7 | Pregelatinised maize starch |
| 8 | Maize Starch |
| 9 | Sodium Starch Glycolate |
| 10 | Stearic acid |

**Packaging:**

| Strength | Packs available |
|---|---|
| 220mg | HDPE container (CRC),100CC |

## Physicochemical Evaluation of Aleve 220 tablets:

**Description** : Blue Colored, Oval shaped, biconvex film coated tablet, debossed with 'ALEVE' on one side and other side.

**Avg. Weight** : 300.0mg

**Strength** : 220mg

**Length** : 12.0mm

**Width** : 7.4mm

**Thickness** : 4.50-5.00mm

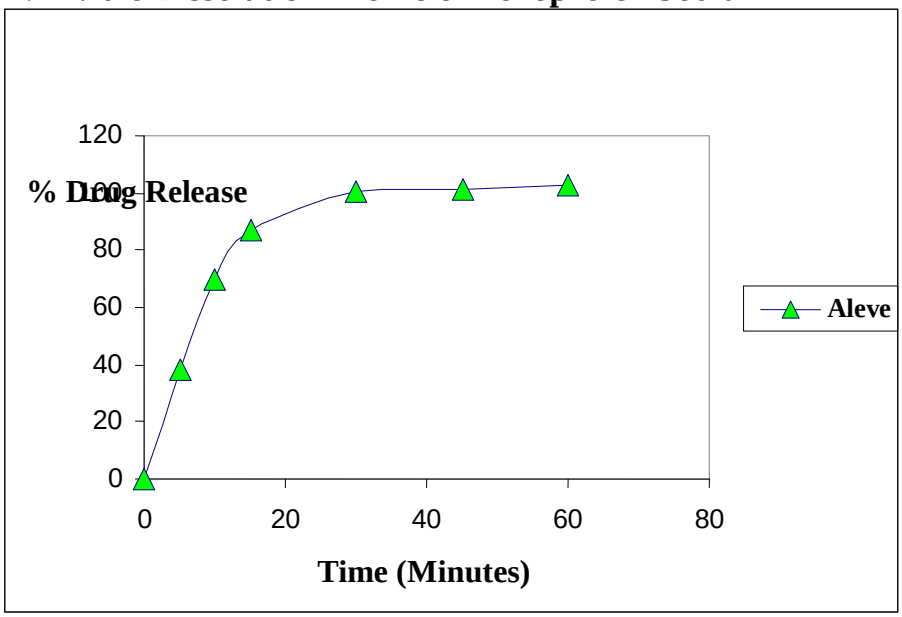
**Hardness** : 5.0-12.0kp

**DT** : 12.30min

**Table -2 : Dissolution Data**

| Time (min) | % Drug Release |
|---|---|
| 5 | 37.90 |
| 10 | 69.60 |
| 15 | 86.90 |
| 30 | 100.80 |
| 45 | 101.60 |
| 60 | 102.80 |

Fig -1 : **Invitro Dissolution Profile of Loxoprofen Sodium**



# MATERIALS AND EQUIPMENTS USED

## Materials Used

The following were the list of excipients selected for the formulation, but the finalized list of excipients were based on the innovator product:

**Table -3 : List Of Excipients Selected For The Formulation**,

| S.No | Ingredients used | Category |
|---|---|---|
| 1 | Loxoprofen Sodium | Active |
| 2 | Maize Starch | Binder/diluents |
| 3 | Pregelatinized Maize Starch | Binder/diluents |
| 4 | Micro crystalline cellulose (MCC) | Diluent |
| 5 | Sodium Starch Glycolate(SSG) | Disintegrant |
| 6 | Povidone K-30 | Binder |
| 7 | Stearic acid | Lubricant |
| 8 | Purified Water | Vehicle |
| 9 | Aquarius BP 17066 | Coating Material |
| 10 | Purified water | Solvent |

**Microcrystalline Cellulose[9]**

| | |
|---|---|
| Synonyms | Celex, Avicel PH, crystalline cellulose |
| Chemical Name | Cellulose |
| Empirical Formula | $(C_6H_{10}O_5)n$ |
| Functional Category | Adsorbent, diluent, disintegrant |
| Description | It is purified, partially depolarized cellulose that occurs as white, odorless, crystalline powder composed of porous particles. |
| Uses of MCC | Use — concentration (%)<br>Adsorbent — 20-90<br>Antiadherent — 5-20<br>Capsule binder/diluent — 20-90<br>Tablet disintegrant — 5-15<br>Tablet binder/diluent — 20-90 |
| Melting Point | $260\text{-}270^0$ C |
| Moisture Content | Less than 5% |
| Solubility | Slightly soluble in 5% w/v hydroxide solution; practically soluble in water, dilute acids, and most organic solvents. |
| stability and storage | It is a stable through hygroscopic material. Bulk material should be stored in a well – closed container in a cool, dry place. |
| Incompatibilities | Incompatible with strong oxidizing agents |
| Safety | Non toxic and non irritant material |
| Precautions | It may be irritant to the eyes. So gloves, eye protection, and dust mask are recommended. |
| Regulatory status | GRAS listed. |

## Sodium Starch Glycolate[9]

| | |
|---|---|
| Synonyms | Carboxy methyl starch, sodium salt, explotab, primojel. |
| Chemical Name | Sodium carboxymethyl starch |
| Empirical Formula | The USPNF 20 states that sodium starch glycolate is the sodium salt of a carboxymethyl ether of starch. |
| Concentration use of sodium starch glycolate | 2-8% |
| Functional Category | Tablet and capsule disintegrant. |
| Description | Sodium starch glycolate is a white to off-white, odorless, tasteless, free-flowing powder. It consists of oval or spherical granules, 30-100 um in diameter, with some less-spherical granules ranging from 10-35 um in diameter. |
| Melting Point | Does not melt, but chars at approximately 200° C |
| Swelling Capacity | In water, sodium starch glycolate swells to up 300 times its volume. |
| Solubility | Sparingly soluble in ethanol (95%), practically insoluble in water. At a concentration of 2 % w/v sodium starch glycolate disperses in cold water and settles in the form of a highly hydrated layer. |
| Incompatibilities | Sodium starch glycolate is incompatible with ascorbic acid. |
| Safety | Nontoxic and nonirritant material. However, oral ingestion of large quantities may be harmful. |
| Related substances | Pregelatinized starch, starch. |
| Stability and Storage Conditions | Tablets prepared with Sodium starch glycolate have good storage properties. Sodium starch glycolate is stable and should be stored in a well-closed container in order to protect it from wide variations of humidity and temperature, which may cause caking .<br>The physical properties of Sodium starch glycolate remain unchanged for up to 4 years if it is stored at moderate temperatures and humidity. |
| Regulatory status | Including in the FDA Ingredients Guide (oral capsules and tablets). |

## Povidone K-30[9]

| | |
|---|---|
| Synonyms | Kollidone, pvp, plasdone |
| Chemical Name | 1-Ethyl-2-pyrrolidinone homopolymer |
| Empirical Formula | $(C_6H_9NO)n$ |
| Functional Category | Disintegrant, dissolution aid, suspending agent, tablet binder. |
| Uses of Povidone | Use — concentration (%)<br>Carrier for drugs — 10-25<br>Dispersing agent — up to 5<br>Eye drops — 2-10<br>Suspending agent — upto5<br>Tablet binder, tablet diluent, or coating agent — 0.5-5 |
| Description | It occurs as a fine, white to creamy – white colored, odorless or almost odorless, hygroscopic powder. |
| Melting Point | Softens at 150°C |
| Moisture Content | It is very hygroscopic |
| Solubility | Freely Soluble In Acids, Chloroform, Ethanol, ketone And Water; practically insoluble in ether, hydrocarbons, and mineral oil. |
| Stability and Storage Conditions | Povidone darkens to some extent on heating at 150°C, with a reduction in aqueous solubility. It is stable to a short cycle of heat exposure around 110-130° C, steam sterilization of an aqueous solution does not alter its properties. |
| Incompatibilities | Povidone is compatible in solution with a wide range of inorganic salts, natural and synthetic resins, and other chemicals. It forms molecular adducts in solution with sulfathiazole, sodium salicylate, salicylic acid, Phenobarbital, tannin, and other compounds. The efficacy of some preservatives, e.g. Thimersol, may be adversely affected by the formation of complexes with povidone. |
| Safety | It is nontoxic, nonirritant and it is not absorbed from the GI or mucous membranes. |
| Related substances | Crospovidone |

## Stearic acid :[9]

| | |
|---|---|
| Synonyms | Crodacid,Hystreme,Pristerene |
| Chemical Name | Octadecanoic acid |
| Empirical Formula | $C_{18}H_{36}O_2$ |
| molecular weight | 284.47 |
| Functional Category | Emlsifying agent,solublizing agent,tablet & capsule lubricant. |
| Concentration Used | Ointment &creams-1-20%<br>Tablet lubricant-1-3% |
| Description | It is a hard, white or yellow colored,somewhat glossy,crystalline solid or a white or yellowish white powder.It has a slight odor & taste suggesting tallow. |
| Melting Point | $\geq 54^{o}C$ |
| Moisture Content | - |
| Solubility | Freely soluble in benzene,carbon tetrachloride,chloroform & ether;soluble in ethanol,PEG & hexane,practically insoluble in water. |
| Incompatibilities | It is incompatible with most metal hydroxides & may be incompatible with oxidizing agents. |
| Safety | Nontoxic |
| Regulatatory acceptance | GRAS listed |
| Related substances | Calcium stearate, Magnesium stearate, zinc stearate |
| Stability and Storage Conditions | Magnesium stearate is stable and should be stored in a well-closed container in a cool, dry place. |
| Stability and Storage Conditions | It is a stable material,an antioxidant may be added. |
| Regulatory status | Including in the FDA Ingredients Guide (oral capsules and tablets). |

## Pregelatinised Maize Starch[9] :

| | |
|---|---|
| Synonyms | Compressible Starch, Lycatab C, Lycatab PGS, Mrigel, Starch 1500 G, Pharma Gel. |
| Chemical Name | Pregelatinized Starch |
| Empirical Formula | $C_6H_{10}O_5$ |
| Molecular Weight | 300-1000 |
| Functional Category | Tablet and capsule diluent; tablet and disintegrant; tablet binder. |
| Uses of pregelatinized starch | Use concentration (%)<br>Diluent(hard gelatin capsule) 5-75<br>Tablet binder (direct compression) 5-20<br>Tablet binder (wet granulation) 5-10<br>Tablet disintegrant 5-10 |
| Description | Pregelatinized Starch occurs as a moderately coarse to fine, white to off-white colored powder. It is odorless and has a slight characteristic taste.<br>Examination of Pregelatinized Starch as slurry in cold water, under a polarizing microscopic, reveals no significant ungelatinized granules, no "maltese crosses" characteristic of the starch birefringence pattern. |
| Moisture Content | Pregelatinized Starch is hygroscopic. |
| Solubility | Practically insoluble in organic solvents. Slightly soluble in cold water, depending upon the degree of pregelatinization. Pastes can be prepared by sifting the Pregelatinized Starch into stirred, cold water. Cold water-soluble matter for partially Pregelatinized Starch is 10-20%. |
| Incompatibilities | - |
| Safety | Pregelatinized Starch and starch are widely used in oral solid dosage formulations. Pregelatinized Starch is generally regarded as a nontoxic and nonirritant excipient. However, oral consumption of massive amounts of Pregelatinized Starch may be harmful. |
| Related substances | Starch, sterilizable maize. |
| Stability and Storage Conditions | Pregelatinized Starch is a stable but hygroscopic material, which should be stored in a well-closed container in a cool, dry place. |

## Equipments Used:

| S.No. | Name of Instrument | Manufacturing Company |
|---|---|---|
| 1 | Automatic tablet dissolution apparatus USP I | Pharma Test |
| 2 | Electronic thickness measurement apparatus | Mitutoyos |
| 3 | Friability tester USP 23 | Electro Lab |
| 4 | Tablet hardness tester | Pharma Test |
| 5 | Electronic LOD measurement apparatus (Halogen Moisture Analyzer) | Mettler Toledo |
| 6 | Tap Density Apparatus USP | Electro lab, |
| 7 | Electronic weighing balance, 150 Kg | Mettler Toledo, |
| 8 | Electronic weighing balance, 6 Kg | Mettler Toledo |
| 9 | Electronic weighing balance, 300 Gms | Mettler Toledo, |
| 10 | Lab stirrer 8 Liters | Eltech |
| 11 | Single Deck Sifter | SWECO |
| 12 | Octagonal Blender 10 Liters | Saan |
| 13 | Tablet compression machine 12 station | RIMEK – minipress |
| 14 | Fluid Bed Processor (FBP) FBE – 5 | P+am Glatt |
| 15 | Tablet Coating Machine (Neocota – 5 kg) | Neomachines |
| 16 | Moisture Content ( KF Titrino ) | Metrohm |
| 17 | UV – Spectrometer | Shimadzu |
| 18 | HPLC | Waters – alliance |
| 19 | Disintegration Test Apparatus | Electro lab, |
| 20 | Rapid Mixer Granulator | Sainath Boilers & Pneumatics |
| 21 | Electronic Sieve shaker | SWECO |
| 22 | pH meter | Polmon |

# EXPERIMENTAL WORK

## PREFORMULATION STUDIES[6,10]

Preformulation testing is an investigation of physical and chemical properties of a drug substance alone and when combined with excipients. It is the first step in the rational development of dosage forms.

***Description and solubility*:**

Loxoprofen Sodium is white to off white powder, practically insoluble in water and melt at 105ºc.

***Determination of bulk density and tapped density***

Density is defined, as the ratio of mass to the volume. The density of a powder sample is usually referred to as bulk density, and the volume includes both the particulate volume and the pore volume. The bulk density will vary depending on the packing of powder, several values can be quoted.

Bulk density is when the volume of the powder is at maximum, caused by aeration, just prior to complete breakup of the bulk. Tapped density is the maximum bulk density that can be achieved without deformation of the particles. In practice, it is generally unrealistic to attain this theoretical tapped density, and a lower value obtained after tapping the sample in a standard manner is used.

The bulk density, and tapped density were calculated using the following formulas:

| Bulk density $(B.D) = W / V_o$ |
|---|

| Tapped density $(T.D) = W / V_f$ |
|---|

Where,

W = weight of the powder

$V_O$ = intial volume

$V_F$ = final volume

## Compressibility Index*:*

The compressability index is indirectly related to relative flow rate, cohesiness and particle size of the powder. The compressability index of material can be estimated from the tapped and bulk density of power.

%Compressability index = [(T.D – B.D) / T.D] 100

Where T.D and B.D are bulk density and tap density respectively.

**CARR'S INDEX:**

| COMPRESSIBILITY | FLOW DESCRIPTION |
|---|---|
| 5-15 | Excellent |
| 12-1 | Good |
| 18-21 | Fair |
| 23-28 | Poor |
| 28-35 | Moderately Poor |
| 35-38 | Very poor |
| >40 | extremely poor |

**HAUSNERS RATIO:**

It indicates the flow properties of a powder; it is measured by ratio of tapped density to bulk density

$$\text{Hausner's Ratio} = \frac{\text{TappedDensity}}{\text{Bulk Density}}$$

.

| Hausners ratio | Type of flow |
|---|---|
| Less than 1.25 | Good flow |
| 1.25-1.5 | Moderate flow |
| More than 1.5 | Poor flow |

## SIEVE ANALYSIS:

The main aim of sieve analysis is to determine the different sizes of particles present in the mixture. A series of standard sieve were stacked one above the other so that sieves with larger pore size (less sieve number) occupy top position followed by sieves of decreasing pore size (larger sieve number towards the bottom)

**Procedure:** A series of sieves were arranged in the order of their decreasing pore diameter (increasing sieve number) i.e. sieve number 40, 60, 80, 100, 120, 200, 325# and pan. 100 grams of drug was weighed accurately and transferred to sieve 40 which were kept on top. The sieves were shaken for about 5-10 minutes. Then the drug retained on each sieve was taken, weighed separately and amount retained was expressed in terms of cumulative percentage retained.

| Particle size | % cum. Retention |
|---|---|
| 40# | 6.0 |
| 60# | 11.2 |
| 80# | 14.0 |
| 100# | 15.2 |
| 200# | 18.0 |
| 325# | 22.8 |
| Pan | 77.2 |

## DRUG EXCIPIENT COMPATIBILITY STUDIES

Compatibility studies are carried out to study the possible interactions between Loxoprofen Sodium and other inactive ingredients.

**Procedure:** The compatibility studies were carried out by taking a mixture of drug and excipients at the ratio in which they are expected to be present in the innovator product. A part of mixture can be exposure to different storage conditions like $40^{o}C/75\%$ RH, $30^{o}C/60\%$RH and control samples were to be kept at $2\text{-}8^{o}C$. They were tested with respect to their physical and chemical aspects.

Table-4: Drug Excipient Compatibility studies

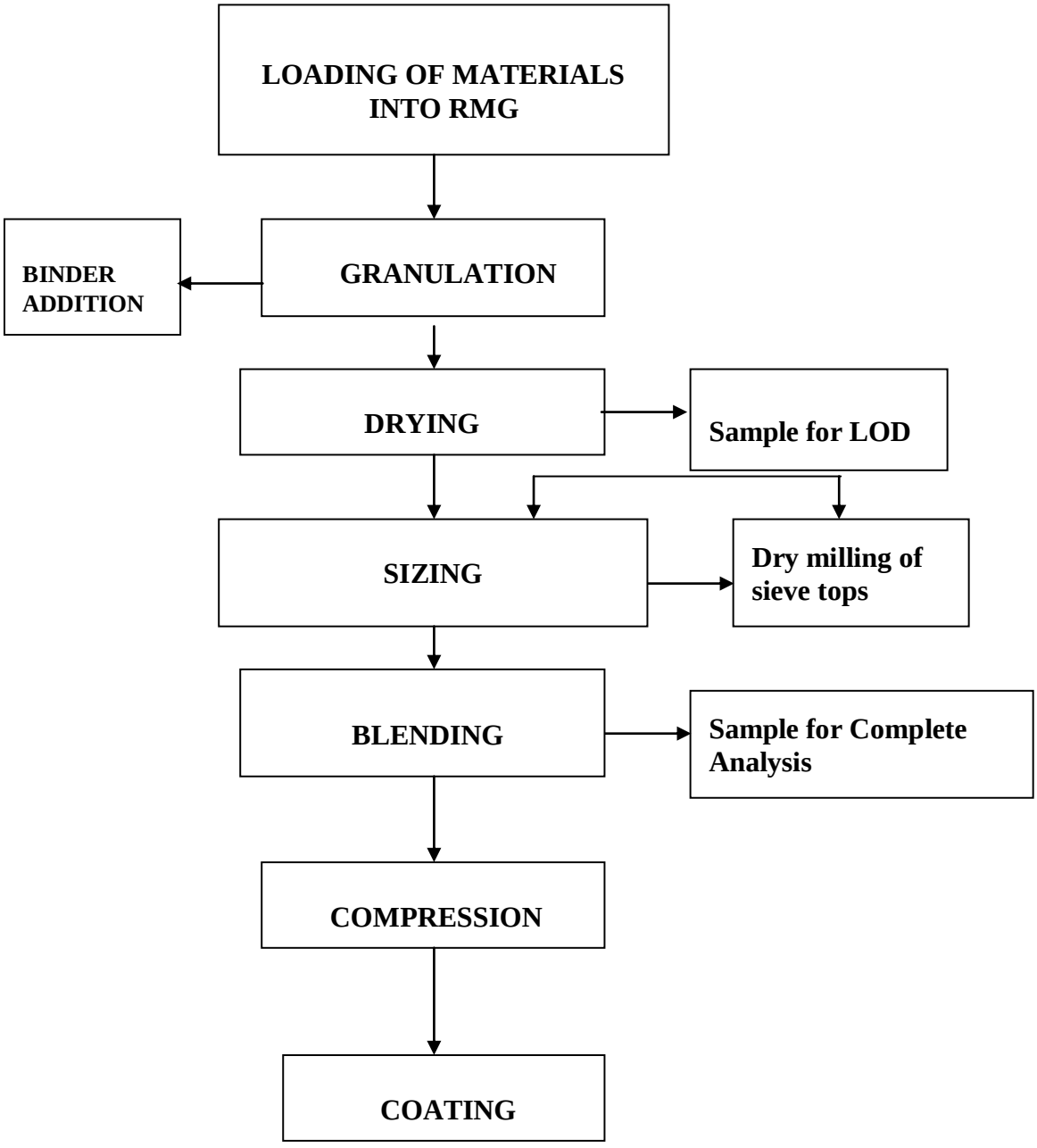
| S.No | Condition | Samples packed in | Samples obtained at |
|---|---|---|---|
| 1 | Accelerated<br>40$^{o}$C/75% RH | 3 Double polythene bags | 1M, 2M, 3M |
| 2 | Intermediate<br>30$^{o}$C/60%RH | 2 glass vessels | 15 days, 30 days |
| 3 | Refrigeration 2-8$^{o}$C | 1 Double polythene bag +<br>1 glass vessel | 3M |

Table-5:

| **Sr. No** | **Name of the Excipient** | **Category** | **Compatibility status with LOXOPROFEN SODUM** |
|---|---|---|---|
| 1 | Microcrystalline cellulose (MCC) | Diluent | Compatible |
| 2 | Maize Starch | Diluent | Compatible |
| 3 | Pregelatinized Maize Starch | Diluent | Compatible |
| 3 | Povidone K-30 | Binder | Compatible |
| 4 | Sodium Starch Glycolate(SSG) | Disintegrant | Compatible |
| 5 | Stearic acid | Lubricant | Compatible |
| 6 | Purified Water | Vehicle | Compatible |
| 7 | Aquarious BP 17066 | Coating material | Compatible |

**DEVLOPMENTAL DESIGN OF LOXOPROFEN SODIUM TABLETS**

Process Flow Chart for Manufacturing of Loxoprofen Sodium Tablets:



**MANUFACTURING PROCEDURE:**

## Granulation:

**Dry Mixing*:***

Load Loxoprofen sodium into RMG along with diluent and mixed for 5 min at slow mixer speed.

**Preparation of Binder Solution:**

Dissolve the binder in hot Purified water. Stir with SS paddle till complete Povidone goes into solution.

**Wet Granulation:**

Add binder into RMG while mixing at slow mixer speed. Add extra water till required consistency of mass is obtained.

**Drying:**

Start the FBP in manual mode & set process parameters as given below. Dry the wet granules at $105^0$C till a LOD of 0.5%w/w – 1.0 %w/w is achieved. (Actual limit established during the trials). Unload the granules. Record all the parameters of fluid bed processor from the process record sheet.

**Sifting:** Sift the dried granules through # 18 mesh.

**Blending and Lubrication:**

Load the sifted granules into Octagonal blender, Lubricant is added into blender by sifting it in 40 mesh and blended for 5 min at 8 rpm.

**COMPRESSION:**

Compress the blend into tablets using 12.0 × 7.3 mm punches and suitable dies with a tablet weight of 300.0 mg.

**COATING:**

Coat the tablets to get 2.5 % buildup by using 15% coating solution. Maintain the following parameters during coating:

Inlet temperature: 50-$60^0$c

Bed temperature: 45-$50^0$c

Spray rate-6gm/min.

Spray pump rpm-6

Automization air pressure-1.8 bar

Gun to bed distance-11.5cm

## FORMULATION DEVEL0PMENT:

**Trial: 1**

**I. Objective:** To manufacture Loxoprofen Sodium Tablets:

**II. Batch size:** 2.0 kg.

**III. Table-6: Formula**

| S.No | Ingredients | % Comp | Qty/Batch(kg) |
|---|---|---|---|
| | Dry mix | | |
| 1 | Loxoprofen Sodium | 73.33 | 1.466 |
| 2 | Maize starch | 20.57 | 0.412 |
| 3 | Pregelatinised starch | 3.6 | 0.072 |
| 4 | Sodium Starch Glycolate | 1.2 | 0.024 |
| | Binder | | |
| 5 | Povidone k-30 | 0.5 | 0.010 |
| 6 | Purified water | QS | 900 |
| | Lubricants | | |
| 7 | Stearic acid | 0.8 | 0.016 |
| Total | | 100.0 | 2.0 |

**IV. Procedure:**

The granulation and compression procedure is same as mentioned earlier.

**V. Observation/Conclusion:**

Granules were not found.

**VI. Further Plan of action:**

Another batch is planned by PVP-K 30(0.7%), Maize starch (20.37%), PGMS(3.2%) SSG(1.6%).

**Trial: 2**

**I. Objective:** To manufacture Loxoprofen Sodium Tablets by taken PVP-K 30 (0.7).

**II. Batch size:** 2.0 kg.

**III. Table-7: Formula:**

| S.No | Ingredients | % Comp | Qty/Batch(gm) |
|---|---|---|---|
| | Dry mix | | |
| 1 | Loxoprofen Sodium | 73.33 | 1.466 |
| 2 | Maize starch | 20.37 | 0.408 |
| 3 | Pregelatinised starch | 3.2 | 0.064 |
| 4 | Sodium Starch Glycolate | 1.6 | 0.032 |
| | Binder | | |
| 5 | PVP K-30 | 0.7 | 0.014 |
| 6 | Purified water | QS | 900 |
| | Lubricants | | |
| 7 | Stearic acid | 0.8 | 0.016 |
| Total | | 100.0 | 2.0 |

**IV. Procedure:**

The granulation and compression procedure is same as mentioned earlier.

**V. Observation/Conclusion**:

Poor flow was observed, compression was not done.

**VI. Further plan of action:**

Another batch is planned by taking Maize starch (21.37%), PGMS (2%), SSG (2%)

**Trial: 3**

**I. Objective:** To prepare Loxoprofen Sodium Tablets by taking Maize starch (21.37%), PGMS (2%), SSG (2%)

**II. Batch size:** 2.0 kg.

**III. Table-8: Formula:**

| S.No | Ingredients | % Comp | Qty/Batch(gm) |
|---|---|---|---|
| | Dry mix | | |
| 1 | Loxoprofen Sodium | 73.33 | 1.466 |
| 2 | Maize starch | 21.37 | 0.428 |
| 3 | Pregelatinised starch | 2.0 | 0.040 |
| 4 | Sodium starch glycolate | 2.0 | 0.040 |
| | Binder | | |
| 5 | Povidone k-30 | 0.5 | 0.010 |
| 6 | Purified water | QS | 900 |
| | Lubricants | | |
| 7 | Stearic acid | 0.8 | 0.016 |
| Total | | 100 | 2.0 |

**IV. Procedure:**

The granulation and compression procedure was same as mentioned earlier.

**V. Observation/Conclusion:**

Poor flow of granules was found and Rat holding was observed during compression.

**VI. Further plan of action:**

Another batch is planned by taking Micro crystalline cellulose (21.17%), PVP K30 (0.7%)

**Trial: 4**

**I. Objective:** To prepare Loxoprofen Sodium Tablets by taking Micro crystalline cellulose (21.17%), PVP K 30 (0.7%).

**II. Batch size:** 2.0 kg.

**III. Table-9: Formula:**

| S.No | Ingredients | % Comp | Qty/Batch(gm) |
|---|---|---|---|
| | Dry mix | | |
| 1 | Loxoprofen Sodium | 73.33 | 1.466 |
| 2 | Micro crystalline sodium | 21.17 | 0.425 |
| 3 | Pregelatinised starch | 2.0 | 0.040 |
| 4 | Sodium starch glycolate | 2.0 | 0.040 |
| | Binder | | |
| 5 | Povidone k-30 | 0.7 | 0.014 |
| 6 | Purified water | QS | 900 |
| | Lubricants | | |
| 7 | Stearic acid | 0.8 | 0.016 |
| Total | | 100.0 | 2.0 |

**IV. Procedure:**

The granulation and compression procedure is same as mentioned earlier.

**V. Observation/Conclusion:**

Better granules were observed and DT is not matching with that of innovater.

**VI. Further plan of action:**

Another batch is planned by taking Micro crystalline sodium (10.00%), Maize starch (11.17%).

**Trial: 5**

**I. Objective:** To prepare Loxoprofen Sodium tablets by taking Micro crystalline sodium (10.00%), Maize starch (11.17%).

**II. Batch size:** 2.0 kg.

**III. Table-10: Formulation:**

| S.No | Ingredients | % Comp | Qty/Batch(kg) |
|---|---|---|---|
| | Dry mix | | |
| 1 | Loxoprofen sodium | 73.33 | 1.466 |
| 2 | Micro crystalline sodium | 10.00 | 0.200 |
| 3 | Maize starch | 11.17 | 0.224 |
| 4 | Pregelatinised starch | 2.0 | 0.040 |
| 5 | Sodium starch glycolate | 2.0 | 0.040 |
| | Binder | | |
| 6 | Povidone k-30 | 0.7 | 0.014 |
| 7 | Purified water | QS | 900 |
| | Lubricants | | |
| 8 | Stearic acid | 0.8 | 0.016 |
| Total | | 100.0 | 2.0 |

**IV. Procedure:**

The granulation and compression procedure is same as mentioned earlier.

**V. Observation/conclusion:**

Better granules were observed, but more Disintegration time .

**VI. Further plan of action:**

Another batch is planned by taking Maize starch (11.67%), Micro Crystalline Cellulose (11.50%).

**Trial: 6**

**I. Objective:** To prepare Loxoprofen sodium tablets by taking Maize starch (11.67%), Micro crystalline Cellulose (11.50%).

**II. Batch size:** 2.0 kg.

**III. Formulation:**

**Table-11:**

| S.No | Ingredients | % Comp | Qty/Batch(kg) |
|---|---|---|---|
| | Dry mix | | |
| 1 | Loxoprofen sodium | 73.33 | 1.466 |
| 2 | Micro crystalline cellulose | 11.50 | 0.230 |
| 3 | Maize starch | 11.67 | 0.234 |
| 4 | Sodium starch glycolate | 2.0 | 0.040 |
| | Binder | | |
| 5 | Povidone k-30 | 0.7 | 0.014 |
| 6 | Purified water | QS | 900 |
| | Lubricants | | |
| 8 | Stearic acid | 0.8 | 0.016 |
| Total | | 100.0 | 2.0 |

**IV. Procedure:**

The granulation and compression procedure is same as mentioned earlier.

**V. Observation/conclusion:**

Disintegration time is matching with that of innovator but not the Dissolution profile.

VI. **Plan of action:**

Another batch is planned by taking MCC (11.0%), Maize starch (10.87%), PVP K30 (2%)

**Trial: 7**

**I. Objective:** To manufacture Loxoprofen sodium tablets by taking MCC (11.0%), Maize starch (10.87%), PVP K30 (2%).

**II. Batch size:** 2.0 kg.

**III. Formula:**

**Table-12:**

| S.No | Ingredients | % Comp | Qty/Batch(kg) |
|---|---|---|---|
| | Dry mix | | |
| 1 | Loxoprofen sodium | 73.33 | 1.466 |
| 2 | Micro crystalline cellulose | 11.0 | 0.220 |
| 3 | Maize starch | 10.87 | 0.218 |
| 4 | Sodium starch glycolate | 2.0 | 0.040 |
| | Binder | | |
| 5 | Povidone k-30 | 2.0 | 0.040 |
| 6 | Purified water | QS | 900 |
| | Lubricants | | |
| 7 | Stearic acid | 0.8 | 0.016 |
| Total | | 100.0 | 2.0 |

**IV. Procedure:**

The granulation and compression procedure is same as mentioned earlier.

**V. Observation/Conclusion:**

Disintegration time is satisfactory but dissolution profile is not matching with reference sample.

**VI. Further plan of action:**

Another batch is planned with Maize starch (8.87%), MCC (13.0%).

**Trial: 8**

**I. Objective:** To prepare Loxoprofen sodium tablets with Maize starch (8.87%), MCC (13.0%).

**II. Batch size:** 2.0 kg.

**III. Formulation:**

**Table-13:**

| S.No | Ingredients | % Comp | Qty/Batch(kg) |
|---|---|---|---|
| | Dry mix | | |
| 1 | Loxoprofen sodium | 73.33 | 1.466 |
| 2 | Micro crystalline cellulose | 13.0 | 0.260 |
| 3 | Maize starch | 8.87 | 0.178 |
| 4 | Sodium starch glycolate | 2.0 | 0.040 |
| | Binder | | |
| 5 | Povidone k-30 | 2.0 | 0.040 |
| 6 | Purified water | QS | 900 |
| | Lubricants | | |
| 7 | Stearic acid | 0.8 | 0.016 |
| Total | | 100.0 | 2.0 |

**IV. Procedure:**

The granulation and compression procedure same as mentioned earlier.

**V. Observation/Conclusion:**

Disintegration time is satisfactory but dissolution profile is not matching with reference sample.

**VI. Plan of action:**

Next batch planned with MCC (15%), Maize starch (6.87%).

**Trial: 9**

**I. Objective:** To manufacture Loxoprofen sodium tablets with MCC (15%), Maize starch (6.87%).

**II. Batch size:** 2.0 kg.

**III. Formulation:**

**Table-14:**

| S.No | Ingredients | % Comp | Qty/Batch(kg) |
|---|---|---|---|
| | Dry mix | | |
| 1 | Loxoprofen sodium | 73.33 | 1.466 |
| 2 | Micro crystalline cellulose | 15.0 | 0.300 |
| 3 | Maize starch | 6.87 | 0.138 |
| 4 | Sodium starch glycolate | 2.0 | 0.040 |
| | Binder | | |
| 5 | Povidone k-30 | 2.0 | 0.040 |
| 6 | Purified water | QS | 900 |
| | Lubricants | | |
| 7 | Stearic acid | 0.8 | 0.016 |
| Total | | 100.0 | 2.0 |

**IV. Procedure:**

The granulation and compression procedure is same as mentioned earlier.

**V. Observation:**

DT is satisfactory but percentage drug release is lower than that of innovater sample.

**VI. Further plan of action:**

Next batch planned with MCC (14%), Maize starch (7.87%).

**Trial: 10**

I. **Objective:** To manufacture Loxoprofen sodium tablets with MCC (14%), Maize starch (7.87%).

**II. Batch size:** 2.0 kg

**III. Formula:**

**Table-15:**

| S.No | Ingredients | % Comp | Qty/Batch(kg) |
|---|---|---|---|
| | Dry mix | | |
| 1 | Loxoprofen sodium | 73.33 | 1.466 |
| 2 | Micro crystalline cellulose | 14.0 | 0.280 |
| 3 | Maize starch | 7.87 | 0.158 |
| 4 | Sodium starch glycolate | 2.0 | 0.040 |
| | Binder | | |
| 5 | Povidone k-30 | 2.0 | 0.040 |
| 6 | Purified water | QS | 900 |
| | Lubricants | | |
| 7 | Stearic acid | 0.8 | 0.016 |
| Total | | 100.0 | 2.0 |

**IV. Procedure:**

The granulation and compression procedure is same as mentioned earlier.

**V. Observation/Conclusion:**

The granules produced have good flow property .As the Disintegration time and Dissolution profile were matching with innovater sample.

**VI. Further plan of action:**

Two reproducibility batches are taken.

**Trial: 11 and 12**

**I. Objective:** To manufacture two reproducibility batches of Loxoprofen sodium tablets .

**II. Batch size:** 2.0 kg

**III. Formula:**

**Table-16:**

| S.No | Ingredients | % Comp | Qty/Batch(kg) |
|---|---|---|---|
| | Dry mix | | |
| 1 | Loxoprofen sodium | 73.3 | 1.466 |
| 2 | Micro crystalline cellulose | 14.0 | 0.280 |
| 3 | Maize starch | 7.87 | 0.158 |
| 4 | Sodium starch glycolate | 2.0 | 0.040 |
| | Binder | | |
| 5 | Povidone k-30 | 2.0 | 0.040 |
| 6 | Purified water | QS | 900 |
| | Lubricants | | |
| 7 | Stearic acid | 0.8 | 0.016 |
| Total | | 100.0 | 2.0 |

**IV. Procedure:**

The same granulation and compression procedure is followed.

**V. Observation/Conclusion:**

Physical property of the granules are similar to that of the batch no.10 and the Dissolution profile as well as the chemical properties of the tablets are same as that of batch no.10.

**COMPARATIVE DATA OF VARIOUS FORMULATIONS:**

**Table-17:**

| Trial / Ingredient | T1 | T2 | T3 | T4 | T5 | T6 | T7 | T8 | T9 | T10 |
|---|---|---|---|---|---|---|---|---|---|---|
| | % COMPOSITION | | | | | | | | | |
| Loxoprofen Sodium | 73.33 | 73.33 | 73.33 | 73.33 | 73.33 | 73.33 | 73.33 | 73.33 | 73.33 | 73.33 |
| Maize starch | 20.57 | 20.37 | 21.37 | _ | 11.17 | 11.67 | 11.0 | 13.0 | 15.0 | 14.0 |
| Pregelatinised maize starch | 3.60 | 3.20 | 2.0 | 2.0 | 2.0 | _ | _ | _ | _ | _ |
| Microcrystalline cellulose | _ | _ | _ | 21.17 | 10.00 | 11.50 | 11.0 | 13.0 | 15.0 | 14.0 |
| Sodium starch glycolate | 1.2 | 1.6 | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 |
| PVP K-30 | 0.5 | 0.7 | 0.5 | 0.7 | 0.7 | 0.7 | 2.0 | 2.0 | 2.0 | 2.0 |
| Stearic acid | 0.8 | 0.8 | 0.8 | 0.8 | 0.8 | 0.8 | 0.8 | 0.8 | 0.8 | 0.8 |
| TOTAL | 100 | | | | | | | | | |

**RESULTS AND DISCUSSION:-**

**RESULTS:**

**Compression Parameters:-**

Table No.5 **:** Compress the blend into tablets by using 12.0 x 7.3 mm punches and suitable dies with a tablet weight of 300.3mg.

| TEST | T1 | T2 | T3 | T4 | T5 | T6 | T7 | T8 | T9 | T10 | T11 | T12 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Compression force-kg | 2500-3000 | 2400-3000 | 2300-3000 | 2400-3100 | 1700-2200 | 1800-2300 | 1700-2100 | 1700-2100 | 1700-2200 | 1700-2300 | 1800-2200 | 1800-2200 |
| Hardness(Kp) | 9-11 | 10-11 | 8-9 | 9-10 | 8-10 | 8-10 | 10-11 | 9-11 | 9-10 | 8-10 | 8-10 | 9-10 |
| Thickness-mm | 4.50-4.65 | 4.65-4.75 | 4.60-4.75 | 4.65-4.80 | 4.80-4.95 | 4.80-4.95 | 4.75-4.85 | 4.70-4.85 | 4.80-4.90 | 4.85-4.95 | 4.80-4.90 | 4.85-4.95 |
| Disintegration time –min | 7.30 | 7.06 | 11.15 | 10.53 | 8.58 | 9.01 | 8.34 | 8.51 | 8.47 | 8.54 | 8.53 | 8.57 |
| Friability -%w/w | 0.23 | 0.59 | 0.4 | 0.16 | 0.14 | 0.15 | 0.4 | 0.21 | 0.18 | 0.20 | 0.19 | 0.18 |
| Weight variation-mg | 295-305 | 300-309 | 307-312 | 299-308 | 298-307 | 300-312 | 305-312 | 302-310 | 305-315 | 299-312 | 300-310 | 298-310 |

## COATED TABLET PARAMETERS:

Table no.6**:** coated tablet parameters

| TEST | T10 | T11 | T12 |
|---|---|---|---|
| Hardness-kp | 9-11 | 8-11 | 10-12 |
| Thickness-mm | 4.95 | 4.90 | 4.97 |
| Disintegration time –min | 10.36 | 10.24 | 10.41 |
| Weight variation-mg | 302-315 | 305-315 | 300-315 |

Table no.7: Dissolution data

| **TIME (mins)** | **CUMULATIVE PERCENT DRUG RELEASE (%)** | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | **T1** | **T2** | **T3** | **T4** | **T5** | **T6** | **T7** | **T8** | **T9** | **T10** | **T11** | **T12** |
| 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 5 | 33.25 | 27.46 | 21.31 | 35.33 | 24.96 | 21.32 | 30.66 | 25.57 | 24.82 | 31.2 | 32.8 | 32.3 |
| 10 | 50.68 | 44.74 | 32.64 | 51.24 | 46.76 | 32.17 | 48.45 | 49.68 | 38.95 | 53.6 | 55.2 | 46.8 |
| 15 | 75.62 | 62.10 | 58.21 | 79.11 | 59.47 | 59.09 | 72.04 | 65.49 | 52.14 | 71.2 | 62.8 | 72.8 |
| 30 | 82.51 | 84.45 | 64.54 | 92.21 | 86.88 | 66.70 | 89.34 | 78.64 | 76.31 | 100.4 | 99.8 | 101.7 |
| 45 | 90.25 | 88.48 | 78.90 | 94.98 | 90.36 | 85.68 | 95.69 | 91.45 | 88.49 | 102.3 | 102.5 | 102.8 |
| 60 | - | 90.38 | 84.41 | - | 91.23 | 90.58 | - | 95.10 | 92.62 | 103.5 | 103.2 | 103.5 |

# EVALUATION:

## IN-VITRO RELEASE STUDIES:

***Innovator***

Dissolution medium: Purified water

Volume of medium : 900ml

Apparatus : USP-II (Paddle Type) apparatus.

Speed (RPM) : 50

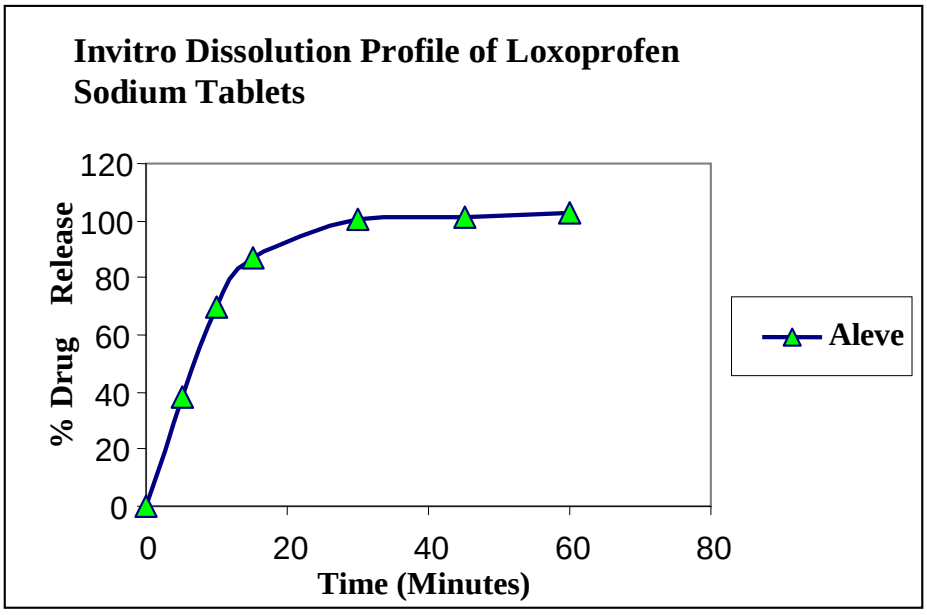
Temperature : 37°C ±0.5°C

Sampling points : 5,10,15,30,45 & 60 min .

**Results:**

| TIME (min) | 5 | 10 | 15 | 30 | 45 | 60 |
|---|---|---|---|---|---|---|
| % Drug release | 37.9 | 69.6 | 86.9 | 100.8 | 101.6 | 102.8 |

**Fig :2. Invitro Dissolution Profile of Loxoprofen Sodium Tablets**



**COMPARATIVE DISSOLUTION STUDIES:**

Dissolution was carried out at following conditions

Dissolution medium: Purified water

Volume of medium : 900ml

Apparatus : USP-II (Paddle Type) apparatus.

Speed (RPM) : 50

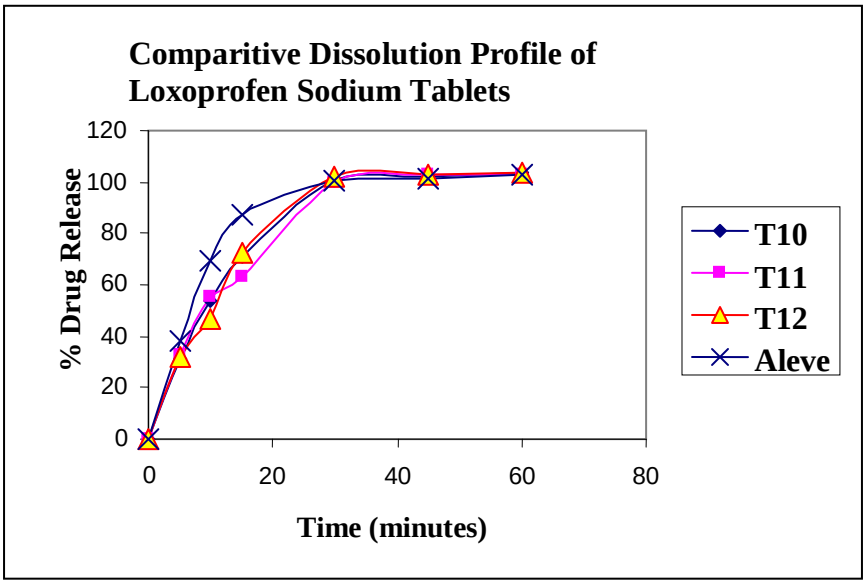
Temperature : 37°C ±0.5°C

Sampling points : 5, 10, 15, 30, 45, and 60 minutes.

**Table:8**

| Time | Innovator | T10 | T11 | T12 |
|---|---|---|---|---|
| 0 | 0 | 0 | 0 | 0 |
| 5 | 37.9 | 31.2 | 32.8 | 32.3 |
| 10 | 69.6 | 53.6 | 55.2 | 46.8 |
| 15 | 86.9 | 71.2 | 62.8 | 72.8 |
| 30 | 100.8 | 100.4 | 99.8 | 101.7 |
| 45 | 101.6 | 102.3 | 102.5 | 102.8 |
| 60 | 102.8 | 103.5 | 103.2 | 103.5 |

**Fig :3. Comparitive Dissolution Profile of Loxoprofen Sodium Tablets**



## DISSOLUTION PROFILE COMPARISON USING $f_1$ $f_2$ FACTORS:

A dissolution profile can characterize the product more precisely than a single point dissolution test. It helps to assure similarity in product performance and signals bioequivalance. The factor $f_1$ is proportional to the average indifference between two profiles, where as factor $f_2$ inversely proportional to the average squared indifference between two profiles. The factor $f_2$ measures the closeness between two profiles, FDA has set a public standard of $f_2$ value between 50-100 to indicate similarity between two profiles.

**F1= ΣD(1/ Σt) x 100**

**F2=1÷ ΣD(1/ Σt) x 100**

## Procedure:

Take the mean dissolution values of the two profiles (test and innovator) which should be

made under same test conditions and same time points. The time points taken as 5,10, 15, 30, 45, 60 minutes. The following mathematical approach is made to compare the dissolution profile using two factors $f_1$ and $f_2$ .

Table no:9

| N | innovator(Rt) | Test (Tt) | D=(Rt-Tt) | $(Rt-Tt)^2$ | F1= Σ D(1/ Σ t)100 |
|---|---|---|---|---|---|
| 5 | 37.9 | 32.8 | 5.1 | 26.01 | |
| 10 | 69.6 | 55.2 | 14.4 | 207.36 | f1=6.1 |
| 15 | 86.9 | 62.8 | 24.1 | 580.81 | |
| 30 | 100.8 | 101.8 | 1.0 | 1.0 | |
| 45 | 101.6 | 102.5 | 0.9 | 0.81 | |
| 60 | 102.8 | 103.2 | 0.4 | 0.16 | F1 = 6.1 |
| n = 5 | Σ Rt=499.6 | | ΣD=49.9 | Σ $(Rt-Tt)^2$ = 816.15 | |

Where:

$f_1$=Dissimilarity factor, $f_2$=Similarity factor

Rt and Tt= Test and innovator cumulative percentage dissolution at selected time points.

N= Number of time point

**Results:**

| Factors | standards | obtained |
|---|---|---|
| $f_1$ | 0-15 | 6.1 |
| $f_2$ | 50-100 | 72.8 |

**Conclusion:** The $f_1$, $f_2$ values of Loxoprofen Sodium Tablets determined as 6.1 and 72.8, there are with in the limits and indicate similarity between two profiles.

**DISCUSSIONS**

- The assay of Loxoprofen Sodium in all trials lies within the limit and complies with the specifications.
- The film coating process was also found to be smooth with no processing problems.
- There is not much variation in the release of drug from the core as well as coated tablets indicating that the coating of tablets to obtain a 2.5% weight gain is found

  to be sufficient to coat the tablets.
- $11^{th}$ and $12^{th}$ are planned for stability study.

# STABILITY STUDIES

Stability studies are an integral part of the drug development program & are one of the most important areas in the registration of pharma products. The purpose of stability testing is to provide evidence on how the quality of a drug substance or drug product varies with time under the influence of a variety of environmental factors such as temperature, humidity & light & enables recommended storage conditions, re-test periods and self half lives to be established. Stability assessment starts with studies on the substance to determine degradation products degradation pathway. In these type of studies the product is analyzed at intervals for various parameters which may include assay of active ingredient, measurement of known degradation products, hardness, disintegration time, dissolution time, appearance etc. Loxoprofen sodium tablets USP 220mg were evaluated for accelerated stability studies at 40ºc/75% RH conditions. Stability details and results presented below

**Storage conditions:** 40ºC/75%RH

**Packs:** HDPE containers

**Period:** 1, 2 & 3 months

Table no: 10

| S.NO | RESULT → TEST ↓ | STABILITY SPECIFICATION | $40^0$C/75%RH | | | |
|---|---|---|---|---|---|---|
| | | | INITIAL | 30 DAYS | 60 DAYS | 90 DAYS |
| 1 | Description | Blue coloured oval shaped, biconvex film coated tablets, debossed with '220' on one side and plain on the other side. | complies | Complies | Complies | Complies |
| 2 | % Drug release | NLT 80% of label claim in 45 min | 99.40 | 99.57 | 99.45 | 99.51 |
| 3 | Assay % w/w | Between 90.0%-110% of label claim. | 100.78 | 100.24 | 99.8 | 99.97 |

# SUMMARY AND CONCLUSION

The main objective of the experimental work undertaken was to develop and evaluate the formulation of Loxoprofen sodium Tablets. The results of the study done are summarized as follows:

1. The tablets manufactured also possessed acceptable parameters almost resembling the market sample.
2. The coating process of the tablets was optimized with a good release of drug from the coated tablets.

From the results it can be concluded that Loxoprofen sodium Tablet was formulated and evaluated . Several trials have been taken to optimize and develop a robust formulation. Various processing problems were encountered during the formulation development and these were overcome with proper optimization of composition of formulation ingredients and processing conditions. The coated tablets were evaluated for the physical as well as chemical attributes and were found to be satisfactory in comparison to the market sample. Two reproducibility batches (T11 and T12) were taken for the finalized batch ie.T10 and were charged for stability studies at accelerated condition. The stability study for 3 months shows that the formulation is stable enough at $40^0$C/75%RH.

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# FUTURE PLAN

The formulation is a robust one and the performance is less likely to be affected by the various factors studied. An excellent in-vitro in-vivo correlation is expected as with respect to reference drug. The stability data is found to satisfactory and so the scale up as well as validation batches can be planned for further progress.

So it can be concluded that the Loxoprofen sodium tablets formulation is robust and stable.

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